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Interaction of DNA Fragmentation Factor (DFF) with DNA reveals an unprecedented mechanism for nuclease inhibition and suggests that DFF can be activated in a DNA-bound state

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Abstract

DNA fragmentation factor (DFF) is a complex of the DNase DFF40 (CAD) and its chaperone/inhibitor DFF45 (ICAD-L) that can be activated during apoptosis to induce DNA fragmentation. Here, we demonstrate that DFF directly binds to DNA in vitro without promoting DNA cleavage. DNA binding by DFF is mediated by the nuclease subunit, which can also form stable DNA complexes after release from DFF. Recombinant and reconstituted DFF is catalytically inactive yet proficient in DNA binding, demonstrating that the nuclease subunit in DFF is inhibited in DNA cleavage but not in DNA binding, revealing an unprecedented mode of nuclease inhibition. Activation of DFF in the presence of naked DNA or isolated nuclei stimulates DNA degradation by released DFF40 (CAD). In transfected HeLa cells transiently expressed DFF associates with chromatin, suggesting that DFF could be activated during apoptosis in a DNA-bound state.

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